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EXAMINER
LOW, C

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 3 June 1991 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire three (3) month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 2-10 are pending in the application.

   Of the above, claims 2-4 are withdrawn from consideration.

2. ☒ Claims 1 have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 5-10 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev.9-89)

The application should be reviewed for errors. The following are examples of the informalities that have been noted: The status of all related applications should be presented in a paragraph at the beginning of the specification. Note that "Thus a" (page 2, line 10) needs a comma inserted; "aminoacid" (page 2, line 23) is by convention, two words; "7000 Ci/mmol" appears to be in error; "Messing" (page 21, line 4) does not need to be underlined; "pertussin" (page 25, line 5); the last 2 lines of Table 5 are illegible; "B. pertussis" (page 32, line 2) needs to be underlined; "acitvity" (page 39, line 7); and "pretussis" (page 40, line 14). The appropriate corrections are required.

The use of the trademarks "LYPHOZYME" (page 7, line 13), "KODAK" (page 7, line 17), "EM" (page 7, line 18), "ELUTIP-D" (page 7, line 22), "Lighting-Plus" (page 11, line 23), "MicroGenie" (page 21, line 11), have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant's election with traverse of the invention of Group I, in Paper No. 4 is acknowledged. The traversal is on the ground(s) that the mutant pertussis toxin proteins of Group II are related and that they are not related (see page 4 of the response to the restriction) is not convincing nor have any reasons been presented showing that a polypeptide can be directly used to produce a DNA or address. Here, and as argued in the response, the protein and the DNA are chemically distinct compositions. Moreover, any manual or "online" search of the available patents and published nonpatent literature such as recognized peer reviewed journals would not be so coextensive as to result in a complete and thorough search for the polypeptides when a search is conducted for DNA or when conducted in the reverse order; and a serious burden has been shown as required by MPEP 803. Note the different areas of search, separate status in the art, non-coextensive search. See the right column of page 800-3 of the MPEP (Rev. 8, May 1988) which states that "For the purposes

of the initial requirement a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 803 and 808.02. Thus, the traverse is not convincing, the requirement is still deemed proper and is therefore, made FINAL.

Claims 5-10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the prior invention as set forth in claim 1 of U.S. Patent No. 4,883,761 in view of Burnette et al. (Science) which discloses analogs of the pertussis toxin where those amino acid alternations would have been coded for by the DNA. It is pointed out that the date of enablement for producing such analogs extends only to the filing date of 15 February 1989 which is the filing date of U.S. application with serial number 07/311,612, now abandoned.

Claims 5-10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the prior invention as set forth in claim 1 of U.S. Patent No. 4,883,761 in view of Burnette et al. (J. Cell. Biochem.) which discloses a recombinant DNA approach to determining the effects of amino terminal truncation of the S1 subunit of the pertussis toxin. Note the region delimited by Tyr8 and Pro14 where " more precise mapping was accomplished by producing a progressive series of amino-terminally truncated recombinant proteins where the testing procedures set forth would reasonably have resulted in the determination of the activity profile of the deletions and where in the alternative, the application of an art recognized process such as site directed mutagenesis would have resulted in producing DNA coding for any amino acid substitution at any of positions 8-14 where only routine testing as indicated in the reference would have been needed to determine the sequence for the DNA coding for the least enzymatic S1 pertussis toxin that retained the appropriate epitope specificity.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of monopoly by prohibiting claims in a second patent not

patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Claims 5-10 are objected to as the terminology "reactogenicity" is undefined and has no apparent antecedent basis in the specification at pages 43-47a which is set forth in the response as supporting the newly presented claims.

Claims 5 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 5, it is not clear how much is "at least a portion" as a dipeptide would apparently have sufficed or which fragment is "at least a portion" and which derivative has an epitope conferring immunoprotection. The terminology "capable of" only recites latent capacity and not that the DNA actually codes for that specific function. Deletion of "capable of" is suggested. Note that the claim terminology permits the alternative interpretation that includes any protein that provides the immunogenic function. How much enzymatic activity corresponds to "substantially reduced", is it 1/2 or .00000001%? What is meant by "reactogenicity"? Note also the objection to the claim.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action :

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent; or

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this

country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 5-10 is rejected under 35 U.S.C. 102 (a) as being clearly anticipated by Burnette et al. (Science) which discloses cloned S1 pertussis gene mutations delineated by the region encoding tyrosine 8 and proline 14 and state that "the most noteworthy S1 analog produced was 4-1 (Arg^{9} Lys)".

Claims 5-10 are rejected under 35 U.S.C. 102 (b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over Burnette et al. (J. Cell. Biochem.) which discloses a recombinant DNA approach to determining the effects of amino terminal truncation of the S1 subunit of the pertussis toxin. Note the region delimited by Tyr8 and Pro14 where " more precise mapping was accomplished by producing a progressive series of amino-terminally truncated recombinant proteins where the test set forth would reasonably have determined the activity profile of the deletion mutations; and where in the alternative, the application of art recognized processes such as site directed mutagenesis would have resulted in DNA coding for any amino acid substitution at any of positions 8-14 where only routine testing as indicated in the reference would have been needed to determine the enzymatic and immunogenic characteristics coded for by that modified DNA which coded for the least enzymatic S1

pertussis toxin that retained the appropriate epitope specificity. Thus, the reference anticipates the invention and if not anticipated, then obvious.

Claim 5-10 are rejected under 35 U.S.C. 103 as being unpatentable over the combination of Locht et al. taken with Burnette et al. (J. Cell. Biochem.). Locht et al. disclose cloning of the pertussis toxin genes and indicate that the S1 subunit is responsible for cellular penetration and the ADP-ribosylation (reference Fig. 2) and while Locht et al. differs from the claimed invention in not explicitly disclosing the specific genetic modifications, Locht et al. nevertheless would have motivated one of ordinary skill in the art to modify the DNA coding for the toxin as Locht et al. state that "The cloned and sequenced pertussis toxin gene will facilitate the development of an efficient and safer vaccine against whooping cough. By comparison to other toxin genes with similar biochemical functions, and by physical identification of the active sites either for the ADP-ribosylation in the S1 subunit ..." such that the Burnette et al. reference which discloses a recombinant DNA approach to determining the effects of amino terminal truncation of the S1 subunit of the pertussis toxin. Note the region delimited by Tyr8 and Pro14 where " more precise mapping was accomplished by producing a progressive series of amino-terminally truncated recombinant proteins where the test set forth would reasonably have determined the activity profile of the deletion mutations; and where in the alternative, the application of art recognized processes such as site directed mutagenesis would have resulted in DNA coding for any amino acid substitution at any of positions 8-14 where only routine testing as indicated in the reference would have been needed to determine the enzymatic and immunogenic characteristics coded for by that modified DNA which coded for the least enzymatic S1 pertussis toxin that retained the appropriate epitope specificity and where in the alternative, the application of an art recognized process such as site directed mutagenesis as indicated in the Locht et al. reference would have resulted in producing DNA coding for any amino acid substitution at any of positions 8-14 where only routine testing as indicated in the Burnette et al. reference would have been needed to determine the sequence for the DNA coding for the least enzymatic S1 pertussis toxin that retained the appropriate

epitope specificity. Thus, the invention as is now claimed was within the ordinary skill in the art to make and use at the time it was made; and, was as a whole, clearly prima facie obvious, especially in the absence of evidence to the contrary.

It is noted that the present specification starting at page 43 with EXAMPLE 1 and Figure 6 contains newly added material related specifically to the genetic mutations which are not accorded the benefit of the parent application having the serial number 06/843,727.

No claim is allowed.

An inquiry concerning this communication should be directed to Christopher Low at telephone number 703 557-0664.

CSF
CSF Low
18 June 1991

Elizabeth C. Weimar

ELIZABETH C. WEIMAR
SUPERVISORY PATENT EXAMINER
ART UNIT 184